J. M. THODAY
Professor of Genetics, University of Cambridge

Causes and Functions of

Genetic Variety *

Introduction

DISCUSSION OF ANY eugenic programme or policy must involve judgement of the relative merit of differing individuals as potential ancestors of future generations. Such value judgements take us into deep philosophical waters into which I have no intention of plunging as I do not believe the biologist is as biologist any better qualified to make such value judgements than anyone else.

The biologist is however qualified to set out the factual and theoretical biological framework that must be taken into account when any such value judgements are made and hence must at least paddle a little at the edge of the philosophical sea when he wishes to expound knowledge he believes to be relevant. Further, the biologist has I think a duty to express the views that arise from his specialized knowledge concerning the biological origin and function of the various characteristics that may or should be considered in relation to any relevant policy. Likewise the sociologist and psychologist should have relevant considerations to put forward, so that final judgement must be based on complex integration: we should expect this, and beware of any specialist who puts forward his own speciality as the only one permitting authority in relation to any particular problem.

My purpose, therefore, is to consider certain biological attributes, especially as they are illuminated by the results of recent researches, from the biological point of view, so as to bring out something of their biological function.

Now in most discussions of this kind, whether at the individual or the population level, the attributes under consideration are the attributes of individuals. We may for instance consider height, or the attribute or attributes that are measured by IQ tests, about which there are two questions the geneticist may be asked. The first is: if for example individuals with higher IQs breed more than those with lower (or vice versa), will the IQ of the population change, and at what rate? The second question is, if we were effectively to encourage such differential reproduction in favour of IQ, what would be the consequent changes in characteristics other than IQ? The first of these questions is of course difficult enough to answer, witness the problem of interpreting the facts concerning correlations of IQ and family size. The second is at present impossible to answer for even if we were to suspect negative correlations between other attributes we deem desirable and IQ, establishment of the facts concerning the degree to which the correlation had genetic causes would be a difficult task indeed.

Difficult though they are, however, it is not this kind of question that I am involved in. I am not concerned with individual attributes but with an attribute which by its very nature the individual cannot possess. What I am concerned with is the variety of individuals in the population, particularly in as much as it arises from genetic variety.

I think this a matter of proper concern in the Eugenics Society, because it is generally to be expected that natural or artificial selection of the ordinary kind will tend to reduce the genetic variety of a population, as also will inbreeding.

We therefore should be prepared to consider the value we put on variety as an attribute of a population as well as the value we put on the average or on individual attributes.

Now when we come to the question of the value we place on variety—particularly genetic variety—we really do come to the shore of stormy philosophical seas. But it is I think just because of this that the specialist's knowledge of the facts of genetic variety and his views concerning the causes and functions of such variety may be of importance, for they may help to limit the field of philosophical discussion.

Genetic Variety

It is a fact that has become more and more clearly and strikingly established in recent years that in natural populations genetic variety is ubiquitous. Much of the most striking evidence comes from studies of flies, but there is quite sufficient evidence from other organisms, including man, for us to generalize. Any natural population of an outbreeding species contains an enormous variety of genetically different individuals.

Much of this variety is fairly readily detected, but much more is variety not readily discernible as affecting the variety of observed characteristics of contemporary individuals: it is what we call cryptic, or concealed, genetic variety and its demonstration depends on relatively sophisticated experiments, or techniques.

There was a time when it was generally expected that a population would be relatively uniform genetically, such variation as there was being due to the usually accidental spread at low frequencies of recently mutated genes. Certain phenomena, however, classed under the heading "polymorphism" (we should speak in this context of "genetic" or "segregational" polymorphisms) stood out as exceptions to the rules upon which this expectation was based. Work aimed at elucidating the causes of genetic polymorphism notably in the hands of Ford's school at Oxford and of Dobzhansky in the United States, together with demonstration of more subtle classes of polymorphism by Dubinin, the work on quantitative inheritance initiated by Mather, and work on blood groups in man and other mammals, have all converged as meaning

that the arguments upon which this expectation of relative genetic uniformity was based were erroneous. On the contrary, when we investigate adequately two homologous chromosomes taken from two individuals of a population of flies we find that they are different, or if we make suitable tests on humans by skingrafting we find that it is only identical twins that are alike. Each individual appears to be genetically unique, and the more we discover about the genetic architecture of natural populations of outbreeding species the more clear it becomes that polymorphisms are not peculiar except as extreme examples of a general phenomenon that does not usually force itself upon our notice but is always there. We begin to feel it is not too much to say that, apart from identical twins, no two individual flies or humans have ever been genetically exactly alike.

Now, though mutation must have provided the variety of genes upon which this diversity depends, it is very clear that recurrent mutation pressure is responsible for the maintenance of only a small part of it and much of that is deleterious. The bulk of this normal genetic diversity must be maintained in the population through other causes, and hence it is clear that diversity itself, albeit no doubt diversity of the proper kind, fulfils an important function in the economy of most natural populations, including populations of humans. Investigation into and discussion of the causes and functions of this natural diversity of course go hand in hand; understanding of the causes throws light on the functions.

We know four explanations of this genetic diversity, which I should stress are not alternative explanations, except in certain specific cases, but involve four kinds of cause each of which probably contributes or has contributed to diversity in any particular population.

The four causes are, slow change of the environment over long periods of time, heterogeneity of the environment in space and over short periods of time, assortative mating, and superior fitness of individuals heterozygous at a particular locus when compared with either of the corresponding homozygotes. I shall not spend time on the last two of these, believing them to be mainly a consequence of the first two.

The first of these explanations stems from the

penetrating discussions by Darlington (1932 and 1939) of the properties of genetic systems. It invokes the fact that all contemporary species have evolved in a slowly changing environment, and that the changes the environment was to undergo in the then future were in essence unpredictable. In these circumstances natural selection would always be tending to promote adaptation to contemporary conditions, and in so far as environmental change was slow, to promote the maintenance of that adaptation. Over long periods of time, however, environmental change would be considerable and to meet it populations must retain adaptability. Now the maintenance of adaptation depends upon stability in heredity, but adaptability depends upon the possibility of hereditary variation. The two requirements, adaptation and adaptability are therefore opposite, and the only populations that will have survived long periods of evolution are those which retained adaptability despite the selection for adaptation, those which developed genetic systems permitting compromise between the two needs. As Mather (e.g. 1943) and I (e.g. 1953) among others have discussed, the development of cryptic genetic diversity such as we find so widespread in natural populations provides a means of doing this efficiently. On this view much of visible diversity is the price we pay for an adaptable genetic system. When the genetic diversity is cryptic that price is reduced. But some price is inevitable for genetic diversity is the prerequisite of genetic adaptability and hence of survival in the novel and unpredictable conditions of the future, though many of the genetic variants will be ill adapted in the present and some will never be of use.

The second explanation has come to the fore more recently as a result of some ideas put forward by Mather (1955), and relevant researches I and my colleagues have carried out over the last seven years. This explanation invokes the fact that the environment to which a population is exposed at any one time is not uniform. On the contrary it would be truer to say that no two individuals meet quite the same environments. This being so, different groups of individuals will be exposed to different selective forces, and natural selection will continually be selecting different parts of a population in slightly different directions.

Selection and Genetic Variety

In these circumstances it would seem reasonable to expect that different genes or constellations of genes might be favoured in the different parts of the population and hence that the diversity of environment would actually give rise to positive selection for diversity of genotype. What remained was to find out by experiment whether this can in fact be an effective factor promoting genetic diversity in populations and, if so, how effective. To this end (Thoday 1959, etc.), I and my colleagues have taken a simple quantitative character—hair number in Drosophila—and exposed populations to selection for and against diversity in this character. It proves that such selection is surprisingly effective.

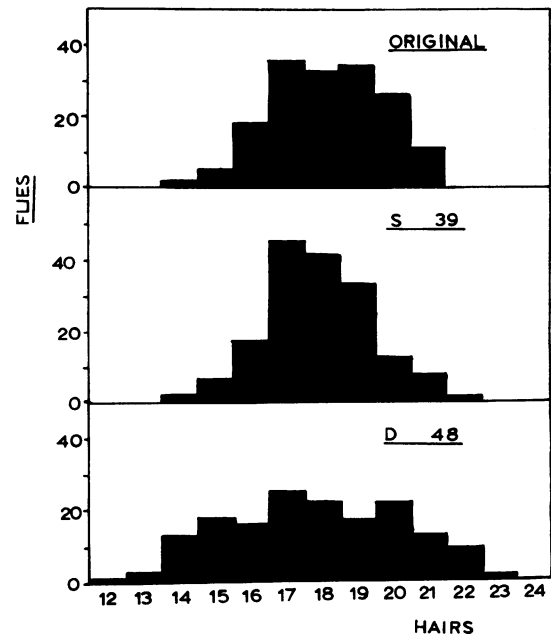Our earliest results are illustrated in Figure 1 which shows the variety of hair numbers in a

FIGURE 1.
The number of flies with each hair-number in samples of 160 flies of the three experimental populations.
Original: the wild stock from which the other populations were derived. S: the stock bred by choosing average flies only as parents for 39 generations. D: the stock bred by choosing both extreme types of fly as parents for 48 generations.

wild stock of flies, together with the variety in two populations selected from that stock in different ways. In one we selected always only the average flies and the consequence is clearly a reduction in the variety of hair numbers. In the other we selected always both extreme kinds of fly, eliminating those near the average and the consequence was increase in the variety of hair number.

Having demonstrated that these results occurred, we were led to ask whether in selecting for and against diversity of hair number in our populations we had in fact brought about change in the adaptability of the populations. Figure 2 shows that we had, for it shows the line selected for the diversity to be more, and that selected for uniformity to be less adaptable than the original wild stock.
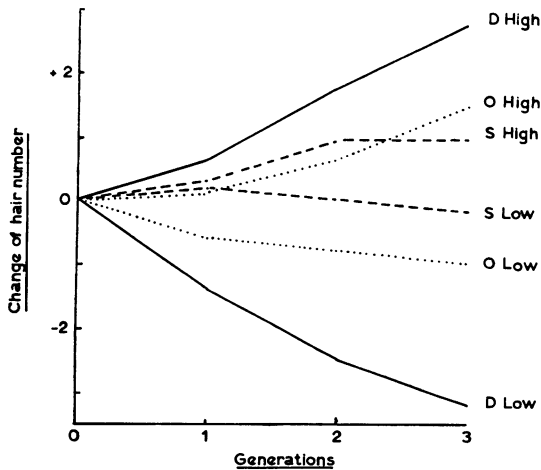

FIGURE 2.

The adaptability of the three populations.

From each population two selection lines were taken, and one was selected for high the other for low hair number. Their rate of divergence measures the adaptability of the population under test. It is clear that the D population is more and the S population is less adaptable than the original (O) wild stock.

We therefore see that such selection does affect the ability of a population to adapt to new conditions. Hence we may extrapolate and reasonably conclude that the heterogeneity of natural environments may preserve and promote the genetic diversity of natural populations, and hence that such diversity will function both as

adapting the population to the diversity of the present environment and as preserving the adaptability of the population against future unpredictable environmental change.

Now it is of some interest in relation to eugenics to consider what we have discovered of the genetic means whereby one of our populations responded to selection for diversity. We (Gibson and Thoday 1962) have made extensive analysis of the genetic constitution of this population, and have shown that part of the diversity is maintained by the maintenance of three alternative classes of chromosome. The first has two low hair number genes $a^L b^L$ upon it, and is responsible when heterozygous with either of the other two, for the flies with few hairs. This chromosome has another property, it is recessive lethal. The other two classes each have one high and one low hair number gene and are $a^H b^L$ and $a^L b^H$. These two classes are indistinguishable except in as much that flies heterozygous for the two, that is $a^L b^H/a^H b^L$ produce by recombination 10 per cent $a^L b^L$ chromosomes among their progeny. These observations put us in a position to test the wild population with which we started and show that it also had both $a^L b^H$ and $a^H b^L$ chromosomes. The first point of interest is that we have here a situation in which a population has adapted to particular conditions by producing and exploiting a lethal chromosome, at the price of course of producing some lethal offspring. Measures taken to reduce the frequency of that "deleterious" chromosome in the population would have been undesirable unless accompanied by measures taken to change the environment in such a way that the "deleterious" chromosome was no longer called for. A similar situation occurs with the sickle cell gene in man which is deleterious, yet in malarial areas advantageous unless the malaria is controlled.

The second point of interest is our demonstration of the cryptic diversity in the wild population. It is notable that the wild population with which we started shows a degree of variety that could be both increased and decreased by selection. This strongly suggests, as we might expect, that there is optimum diversity in any population in any contemporary situation or set of situations. Natural selection tends, as was

demonstrated long ago by Bumpus and by Wheldon, to eliminate extreme variants of all kinds thus stabilizing a population and keeping its properties constant. At the same time, however, it does not eliminate all variants; a proper balance is preserved. But underlying the natural diversity we see in the existence of the two chromosomes a^H b^L and a^L b^H a very clear example of the kind of reserve of variability that Mather in 1943 argued should be there. These two chromosomes differ little in their effects. But their existence together in the population endows it with the capacity of producing extreme recombinants that may be useful as adaptations in the unpredictable future: they endow it with genetic versatility. A price again is paid, for the population must regularly produce some of these recombinants which are undesirable in the present. But the price is reduced by the two genes' association in the same chromosome.

I have now said nearly enough about these causes of variety. But there is one further important point. In our latest experiment (Thoday and Gibson 1962) we selected a wild population for variety under slightly but very significantly different conditions. In this experiment we gave the flies we had selected the opportunity to choose their mates. Thus the more hairy females could choose between equal numbers of more and less hairy males and the less hairy females could choose likewise.

The result of this was as Mather (1955) had predicted. The population rapidly split into two, but it did it with such rapidity that only twelve generations of selection were needed, after which nearly all the effective mating was assortative.

The astonishing rapidity with which this experiment worked raises two questions. The first is: was some assortative mating there in the wild population with which we started? This would suggest that assortative mating might be assisting the wild population to maintain its diversity. We do not know the answer to this for certain yet but preliminary evidence suggests there may be a rather strong tendency for the more hairy flies to choose more hairy and the less hairy to choose less hairy as mates in this wild population.

The second question is more subtle. In the experiment we took a wild population which in the earlier parts of the experiment behaved as a single population. Yet after only a few generations of selection for diversity it was behaving as two separate populations between which hybrids did not or did not often occur. Now this is the sort of process that must be involved in the formation of species, and we are forced to ask: if, in at least this one case, it can be so easy to split a population into two, and given the diversity of natural environments, why is it that it does not happen more often? Why is it for instance that it seems easy to mate *Drosophila melanogaster* populations from all over the world? This suggests that there are compensating disadvantages, forces actually preventing species splitting up in this way. I suggested something of the sort before (Thoday 1953, 1958) and criticised Sir Arthur Keith for assuming speciation to be an essential end of progressive evolution, basing my argument on the view that splitting a population into two produces two populations each genetically less diverse than the original population, and, because less diverse, less genetically versatile. Racial segregationists might take note of this.

Genetic diversity then is produced by the diversity of selective forces operating through variation of the environment in space and in time. It is itself an adaptation, not of the individual but of the species, an adaptation to the unpredictability of the environment; it is responsible for the versatility of populations, their capacity to survive new conditions and even catastrophes such as the myxomatosis epidemic which rabbits have survived. It is one of the most important aspects in the adaptation of populations and species to the conditions of life in our ever changing and variable world.

Conclusion
Now we can be sure that all this applies to man though the situation with respect to man is complicated in a number of ways.

The first complication arises because human populations not only have genetic versatility, but are made up of individuals themselves versatile in many ways. This individual versatility is of course itself a product of the human genotype. Individual versatility is also shown in various

degrees by other organisms, but such individual versatility, the adaptability of the individual to a wide range of environmental conditions, is a property more highly developed in man than any other organism. This comes about of course through the great flexibility of the human brain.

It has itself given rise to the remaining complications, for it has made possible the social development of man through communicated experience, and hence of social inheritance, social evolution and very rapid change of the human environment induced by human activity.

It is sometimes claimed that these factors render unimportant genetic evolution in man, and if this were so, they would render genetic versatility unimportant. However, though I would be the last to under-rate the importance of social inheritance, this individual versatility does not mean that genetic evolution is rendered unimportant. After all, individual versatility itself is a consequence of genetic endowment, and every change social systems produce in human environments necessarily produce consequent genetic changes. Furthermore, no one would pretend that we are in a position, for all our culture, to predict the consequences of our activities for the future. The environment changes more rapidly than ever it did, largely thanks to our own activities, and, though the future is perhaps more predictable to us than it was to our ancestors, this greater rate of change means that the unpredictable aspects of the future will require more rapid adaptation than they did in the past. To say the least, we cannot be sure that our individual versatility is sufficient. Consequently we need to be sure that we attach sufficient importance not only to individual but also to genetic diversity as well as to devising and maintaining flexible social and political systems.

Now in conclusion I should remind you of an important point I made in connection with my experimental results, for the premium I have put in this discussion on the value of genetic variety may seem to suggest that any eugenic policy

designed to reduce the frequency of certain genotypes regarded as undesirable at present, might itself be undesirable as it would tend to reduce genetic variety. This however would be to go too far, for the point the experiment showed was that selection could either increase or decrease variety in the wild population with which we started. The successful population maintains variety, but the variety is limited, there is a balance between too much and too little variety. Uniform populations will be unsuccessful but so are the most extreme variant individuals. Nothing I have said need prevent us from considering eugenic programmes, but we should beware extreme suggestions such as those involving *excessive* multiplication, by asexual reproduction or artificial insemination, of genotypes now considered advantageous. We cannot assess just how much genetic diversity is needed in our complex, variable and ever changing social systems, but we can be sure that it is a good deal. There are always pressures toward uniformity in human populations; to a large extent they should be resisted.

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